Laparoscopic splenectomy for immune thrombocytopenia in patients with a very low platelet count

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Abstract

Introduction: *Laparoscopic splenectomy (LS) is the gold standard in treating immune thrombocytopenia (ITP). However, there are still some problems in decision-making when considering LS in patients with a very low platelet count (PLT).*
Aim: *To evaluate safety outcomes of LS in patients with severe ITP and very low PLT in comparison to those with higher PLT.*
Material and methods: *We retrospectively analyzed consecutive patients who underwent LS in a single institution between April 1998 and December 2017. Perioperative care was based on an algorithm developed at our department which takes into consideration the patient's PLT level. Patients were divided into 2 groups depending on the PLT level (cut-off point 50,000/mm^3).*
Results: *The mean operative time in the low PLT group and high PLT group was 90 ±42.1 min and 95 ±45 min, respectively (p = 0.59). Intraoperative blood loss was 144 ±226.1 ml in the low PLT group and 83 ±161.24 ml in the high PLT group (p = 0.23). Complications occurred in 5 (9.09%) patients in the low PLT group and 16 (11.51%) in the high PLT group (p = 0.67). There were no conversions in the group with lower PLT, while 2 patients in the group with higher PLT had to be converted to open surgery (p = 0.38). Patients with low PLT preoperatively more often required perioperative platelet transfusions (13 vs. 1, p < 0.001).*
Conclusions: *Laparoscopic splenectomy is safe and feasible treatment in patients with ITP regardless of the PLT level. Still, patients with critical ITP and marginally low PLT require special awareness.*

Key words: *laparoscopy, splenectomy, immune thrombocytopenia.*

Introduction

Intra- and postoperative bleeding is one of the more common surgical complications. Its occurrence depends mostly on the type and the extent of the procedure as well as coagulation profile of the patient. In fact, any hematological disorder related to coagulopathy is by definition associated with increased risk of perioperative bleeding. Immune thrombocytopenia (ITP), also known as idiopathic or immune thrombocytopenic purpura, is a relatively common hematologic disease characterized by immune-mediated destruction of platelets, mostly in the spleen, leading to a low platelet count (PLT) and bleeding [1]. Among treatment modalities splenectomy is considered a main second-line treatment in refractory cases that do not respond to conservative management. In 1991, the very first laparoscopic splenecto-

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my (LS) was conducted by Delaitre and Maignien [2]. Since then LS has become the gold standard for patients suffering from ITP and has gradually replaced traditional open splenectomy (OS) [3]. Laparoscopic splenectomy has many benefits such as lower rates of morbidity and mortality, reduced surgical trauma and blood loss, lower postoperative pain, better cosmetic appearance and shorter hospital stay [4]. Uncorrected coagulopathy is considered an absolute contraindication to surgical procedures in general and is particularly strongly emphasized in the case of laparoscopy [5, 6]. There are potential problems in decision-making when considering LS in severe cases of ITP with extreme low PLT. It is commonly accepted that the safe PLT count to perform surgery is 50,000/mm^3, but in patients with ITP it is not always possible to achieve [4]. Therefore, in this study we aimed to evaluate the safety of LS in patients with severe thrombocytopenia.

Aim

The aim of the study was to evaluate safety outcomes of laparoscopic splenectomy in patients with severe ITP and very low PLT in comparison to those with higher PLT.

Material and methods

Consecutive patients undergoing laparoscopic splenectomy for ITP in a university tertiary referral center between April 1998 and December 2017 were included in the study. Before surgery, all patients underwent preoperative assessment and were treated conservatively by a consultant hematologist in order to control the disease and increase platelet levels. In the case of treatment failure or complications related to used medications, patients underwent elective laparoscopic splenectomy despite low PLT. Decision-making about whether to perform an LS was assessed using our internal algorithm. Patients were preoperatively managed depending on the PLT level (Figure 1):

1. Patients with PLT ≥ 50,000/mm^3 were selected for laparoscopic surgery without any additional preoperative means.
2. Patients with PLT < 50,000/mm^3 were reevaluated by hematologists and an attempt to raise platelets to the level ≥ 50,000/mm^3 was undertaken. If successful, patients were treated by LS.
3. Patients in whom the hematologist were able to achieve only a partial response and whose preoperative PLT were between 20,000/mm^3 and 50,000/mm^3 were scheduled for LS after ensuring that the blood bank could deliver platelet transfusions immediately whenever needed. Most of them however did not require transfusions.
4. Patients with preoperative PLT < 20,000/mm^3 despite intensive preoperative conditioning were operated on and platelet transfusions were administered intraoperatively in order to elevate PLT level.

The operative method of choice in our department is a laparoscopic 4-port splenectomy, which was performed as described elsewhere [7]. In some patients single incision splenectomy was performed [8]. None of the patients with ITP was initially operated on with an open approach. In all cases routine hematological treatment was implemented before surgical intervention, and the indications for splenectomy included failure of conservative treatment or side-effects of drugs used that did not allow further therapy. Preoperatively, platelet level was routinely measured within 8 h prior to surgery. For the purpose of statistical analyses patients with preoperative PLT

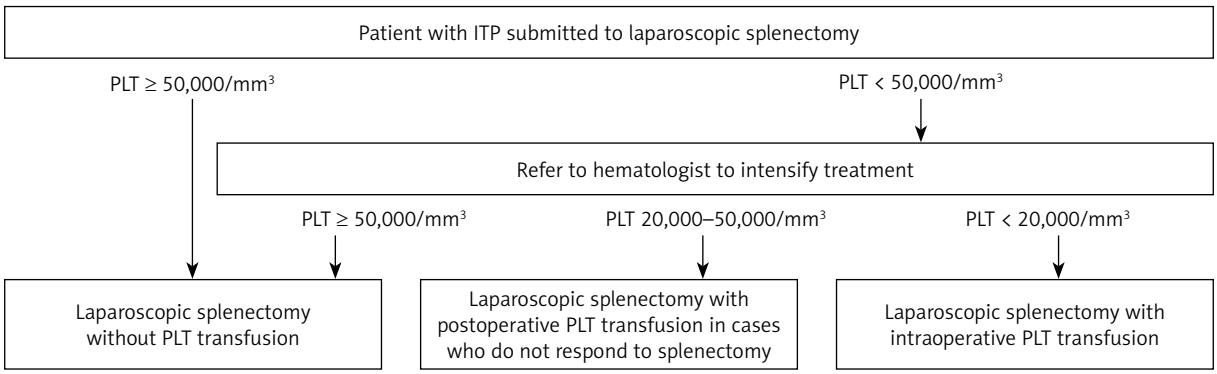

Figure 1. Decision-making algorithm in patients with ITP who underwent laparoscopic splenectomy

< 50,000/mm^3 (low PLT group) were compared with those with PLT ≥ 50,000/mm^3 (high PLT group).

The measured outcomes were the operative time, intraoperative blood loss, need for blood transfusions, conversion rate and morbidity. Operative time was measured from skin incision to closure. The intraoperative blood loss was measured from the amount of blood aspirated in the suction machine. The study was conducted according to STROBE guidelines [9]. All procedures followed the ethical standards of the responsible committee on human experimentation (institutional and national) and the sixth revision (Fortaleza) of the 1975 Declaration of Helsinki. The study was approved by an independent ethics committee of the Jagiellonian University, Krakow, Poland (approval number 1072/6120/160/2017). Informed consent for the surgical treatment was obtained from all patients before the procedure.

Patients

Out of 543 patients undergoing laparoscopic splenectomy in our department in the study period, 194 were operated on for ITP. Group 1 consisted of 9 patients with PLT < 20,000/mm^3. group 2 consisted of 46 patients with PLT ≥ 20,000/mm^3 and PLT < 50,000/mm^3. Group 3 comprised 114 patients with initial PLT < 50,000/mm^3 that was elevated to at least 50,000/mm^3 preoperatively, and group 4 included 25 patients with PLT ≥ 50,000/mm^3. Patients' demographic characteristics are presented in Table I. For the purpose of statistical analyses patients in groups 1 and 2 were combined as the low PLT group and analyzed together with groups 3 and 4 (high PLT group). There were no significant differences in demographics between analyzed groups (Table I).

Statistical analysis

Statistical analysis was performed using StatSoft Statistica version 13.0 software. Normal distribution of continuous variables was tested with the χ^2 test. Variables with non-normal distribution were compared using the Mann-Whitney *U* test. Categorical variables were compared with the χ^2 test. Results

Table I. Demographic data of patients

Parameter	Group 1 (PLT < 20,000/mm^3)	Group 2 (PLT ≥ 20,000/mm^3 and PLT < 50,000/mm^3)	Group 3 (PLT < 50,000/mm^3 elevated to ≥ 50,000/mm^3 before surgery)	Group 4 (PLT ≥ 50,000/mm^3)	*P*-value
	Low PLT group		High PLT group		
Number of patients	9	46	114	25	
	55		139		–
Male/female	5/4	23/23	41/73	5/20	
	28/27		46/93		0.21
Age [years]	43.75 ±16.44	35.96 ±15.73	36.82 ±16.23	39.45 ±16.77	
	40.29 ±17.35		39.98 ±16.5		0.91
PLT	7.5 ±7.93	40.82 ±17.53	130 ±63.16	108.4 ±57.32	
	32.1 ±13.64		118.1 ±59.8		–
Preoperative need for glucocorticoids*	9	41	110	22	
	50		132		0.29
Preoperative need for immunoglobulins*	1	7	18	1	
	8		19		0.87
Preoperative need for PLT transfusions*	5	8	1	0	
	13		1		< 0.001

**Within 7 days prior to surgery.*

were considered statistically significant when the *p*-value was < 0.05.

Results

Patients with low PLT preoperatively more often required perioperative platelet transfusions (13 vs. 1, $p < 0.001$). The mean operative time in the low PLT group and high PLT group was 90 ±42.1 min and 95 ±45 min, respectively. There were no statistically significant differences in this parameter between groups ($p = 0.59$, Figure 2).

Intraoperative blood loss was 144 ±226.1 ml in the low PLT group and 83 ±161.24 ml in the high PLT group – this difference was not statistically significant ($p = 0.23$, Figure 3).

Complications occurred in 5 (9.09%) patients in the low PLT group and 16 (11.51%) in the high PLT group ($p = 0.67$). Characteristics of the complications are presented in Table II. There were no conversions in the group with lower PLT, while 2 patients in the group with higher PLT had to be converted to open surgery ($p = 0.38$). The reasons for conver-

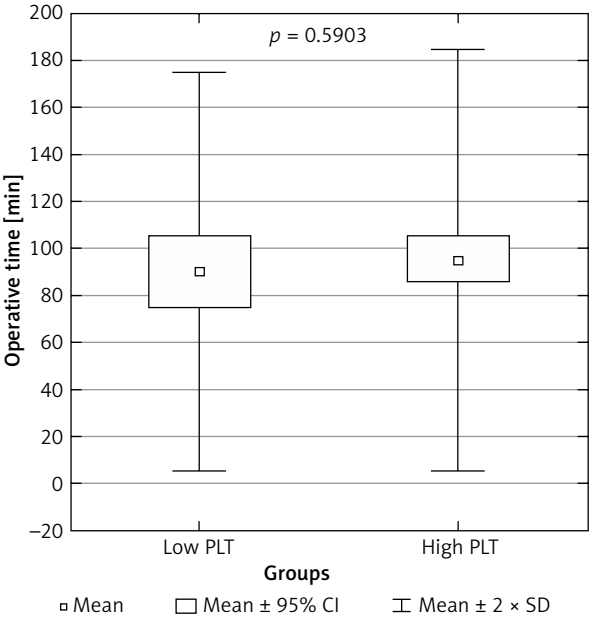

Figure 2. Comparison of the operative time in low PLT group and high PLT group

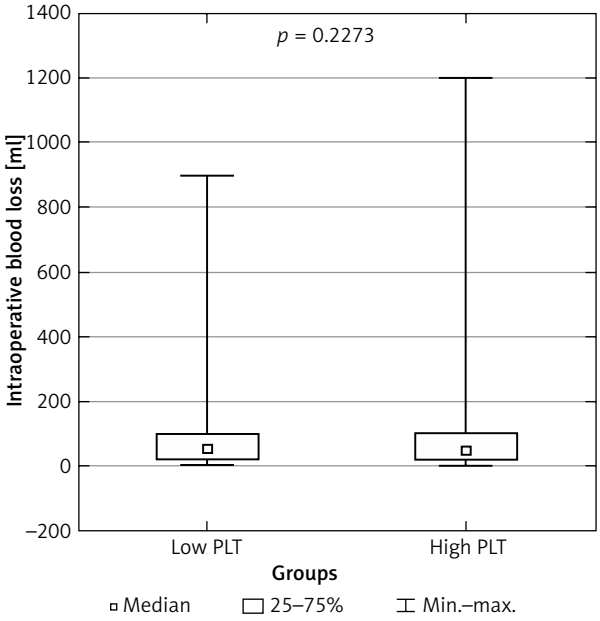

Figure 3. Intraoperative blood loss in low PLT group and high PLT group

Table II. Total complications in both groups according to Clavien-Dindo classification

Clavien-Dindo grade	Complication	Low PLT group ($n = 55$)	High PLT group ($n = 139$)
I	Seroma – fluid collection	0	3 (2.16%)
II	Pneumonia	1 (1.81%)	5 (3.6%)
III a	Hematoma requiring subcutaneous drainage	1 (1.81%)	0
III b	Abscess – required reoperation	1 (1.81%)	2 (1.44%)
	Acute pancreatitis – required reoperation	1 (1.81%)	0
	Bleeding – required reoperation	1 (1.81%)	3 (2.16%)
	Stomach perforation – required reoperation	0	1 (0.72%)
IV b	Abscess – required reoperation	0	1 (0.72%)
V	Pulmonary embolism	0	1 (0.72%)
Total		5 (9.09%)	16 (11.51%)

Table III. Summary of findings

Parameter	Low PLT group	High PLT group	*P*-value
Operative time [min]	90 ±42.1	95 ±45	0.59
Intraoperative blood loss [ml]	144 ±226.1	83 ±161.24	0.23
Complication rate	5 (9.09%)	16 (11.51%)	0.67
Perioperative platelet transfusions	13 (23.6%)	1 (0.7%)	< 0.001

sion were uncontrolled bleeding in both cases: once during splenic hilum dissection and once during mobilization of the spleen. A summary of perioperative results is presented in Table III.

Discussion

We have confirmed that LS in patients with severe ITP and very low PLT is safe and feasible. It is not associated with a different course of surgical procedure or worse postoperative outcomes. In our opinion, the safety of the procedure in patients with end-stage thrombocytopenia might be affected by the strategy of perioperative management developed in our department. It is an important finding since ITP is one of the most common hematologic disorders affecting children and adults with the increasing destruction of platelets caused by the antiplatelet antibodies. Moreover, it is currently the most common indication for non-traumatic splenectomy. The percentage of patients with ITP who will eventually need splenectomy is reported to be, according to large series, as high as 20–45% [10–13].

According to recent a meta-analysis of more than 7,200 patients, LS for non-traumatic diseases of the spleen is superior to OS in terms of reduced blood loss and requirement for blood transfusion, lower morbidity and mortality rates and shorter length of hospital stay [14]. For these reasons, LS is now considered the gold standard for patients with ITP. Although there is a small percentage (7–22%) of patients who do not respond to the treatment, it is still the best option in patients not eligible for conservative management [15].

Preoperative clinical symptoms of thrombocytopenia cause a great risk to patients and are sometimes regarded as a contraindication to surgery depriving patients of an effective method of treatment. Since the spleen in ITP is usually not enlarged, the greatest concern is low PLT that might lead to perioperative hemorrhage, difficulties with hemostasis requiring conversion and subsequent blood transfusions. On one hand it has been proven that LS significantly reduces the blood loss and need for platelet transfusion compared to open surgery [16]. On the other hand, coagulopathy is the absolute contraindication to laparoscopy in most guidelines and it should be corrected before surgery, which for obvious reasons is not possible in the majority of ITP patients [17]. Therefore, according to some authors, LS in low PLT should be contraindicated, whereas PLT higher than 50,000/mm^3 is considered sufficient for effective hemostasis [18–20].

In our study, almost 30% of patients undergoing LS had PLT below 50,000/mm^3 despite the most optimal preoperative management and adjustment of thrombocytopenia. Importantly, we have shown that low PLT is not associated with higher complication rates (complications occurred in 5 (9.09%) patients in the low PLT group and in 16 (11.51%) in the high PLT group). It was achieved with no difference in operative technique. For instance, despite very low PLT we still do not use drains, which according to previous observations do not bring any benefits and in some clinical situations may increase complication rates [21]. This confirms that LS is feasible and safe also in this, theoretically more dangerous, clinical situation. We did not find any statistically significant differences in either complication rates or their severity between groups. Patients with very low PLT did not present an increased rate of perioperative bleeding, which might be related to PLT level. In our study 1 patient from the low PLT group needed relaparoscopy because of bleeding, and 3 patients from the high PLT group. Two of them required conversion. These results are in line with other reports where complication rates were around 10%, with lower morbidity in high-volume centers as noted by Montalvo *et al.* [22]. Although in our study we did not find any relationship between PLT and LS out-

comes, there are previously published reports showing that severe thrombocytopenia might be a risk factor for increased morbidity. For instance, Keidar *et al.* showed that patients with severe thrombocytopenia had significantly more packed red cell transfusions and a much longer stay [23]. Both univariate and multivariate analysis of predictive factors by Duperier *et al.* confirmed that higher preoperative platelet count is associated with a successful response to LS [24].

We did not find any difference between low PLT level and greater difficulty of LS resulting in differences in operative time, increased blood loss or conversion rate. Having said that, the results may be biased because we did not take into account surgeons' experience. It is very likely that the most difficult cases were performed by more experienced surgeons in laparoscopic surgery of the spleen. On the other hand, the operative time in our study was lower than reported elsewhere. Chen *et al.* reported that from a group of 81 patients 9% had massive bleeding, 4 of them requiring conversion to open surgery [1]. Machado *et al.* found in their study that mean blood loss was 70 (range: 50–460) ml and operative time was 126 (range: 110–240) min [25]. In a systematic review Moris *et al.* found that LS can be performed with minimal blood loss (30–60 ml), operative time was reported as 75–165 min, and the conversion rate to OS was in the range 0–4% [26].

In order to establish optimal perioperative management, we developed a simple, easy to follow algorithm (Figure 1) for all surgeons dealing with patients with ITP. Every patient has to be referred by a consultant hematologist who confirms that LS is the optimal treatment of ITP at this stage. In all cases with PLT ≥ 50,000 mm^3 no additional preoperative means of treatment are needed and patients can be operated on safely. In patients whose PLT assessed just before surgery is < 50,000 mm^3, treatment modification is needed. They are referred back to the hematologist for further assessment and potential treatment modification. If hematologic intervention is successful (PLT ≥ 50,000 mm^3) they can undergo LS. Patients with PLT between 20,000 and 50,000/mm^3 despite intensive management and use of all therapeutic options may require platelet transfusions. Therefore 2 packs of platelets should be waiting in the blood bank to be ready for immediate transfusion in patients who do not respond to LS and sustain a low PLT count. Finally, the majority of patients with preoperative PLT < 20,000 mm^2 will require intraoperative PLT transfusions. Therefore, we suggest considering starting transfusion of the first PLT unit at the beginning of the procedure and the next one once the splenic artery has been clipped. Generally the operative strategy is slightly different in those patients. The surgeon should identify, dissect and clip the splenic artery as early in the course of the operation as possible. This maneuver terminates PLT destruction in the spleen in most cases and allows for further dissection. With this strategy we were able to operate even on patients whose PLT level just before surgery was 0. In our study, perioperative platelet transfusions were necessary only in 13 cases (in 6 cases during surgery and in the remaining 7 patients due to failure in PLT elevation postoperatively) in the low PLT group and 1 case in the group with high PLT (the patient did not respond to splenectomy). There are reports suggesting that continuous PLT transfusion may be successful in cases of serious uncontrolled bleeding with PLT below the measurable limit [27].

The limitations of the study are typical for a single retrospective analysis. In addition, we did not analyze other parameters that might influence the outcomes such as body mass index, previous abdominal surgery or the presence of an accessory spleen. Although they might have influenced the outcomes to some extent, none of them were identified as a reason for conversion or massive intraoperative bleeding. Moreover, due to the relatively small number of patients with very severe ITP (PLT < 20,000 mm^3) we were not able to analyze them separately in order to achieve sufficient statistical power.

Conclusions

Our study confirms that LS is a safe and feasible surgical approach in patients with ITP regardless of the preoperative PLT. The procedure is not associated with a longer operative time, increased blood loss or conversion rate. Patients with low PLT are not at risk of increased morbidity. For these reasons, LS should be considered the gold standard in the surgical treatment of ITP. However, special precautions must be taken in the group of patients with severe ITP and extremely low PLT.

Conflict of interest

The authors declare no conflict of interest.

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